

### **REMARKS**

Claims 26, 28-31 and 33-44 are pending pending. Claim 26 has been amended as requested by the Examiner. In particular, the term DNA-dependent has been removed from the claims. In addition, the Brief Description the Drawings has been amended as shown above to further describe the designations used in Figure 6. Finally, the specification has also been amended to insert sequence identifiers. In view of the following remarks and foregoing amendments, Applicants respectfully request reconsideration of the application.

### **Drawings**

Figure 6 was objected to because the sequence was difficult to read. (Office Action, page 2). Applicants submit herewith a replacement sheet for Figure 6 that enlarges the text of the sequence. The legend previously found at the bottom of original Figure 6 has been incorporated into the Brief Description of the Drawings to accommodate the larger text of Figure 6. A annotated sheet is also attached hereto showing the changes made to original Figure 6.

### **Specification**

Submitted herewith is a Sequence listing in compliance with 37 C.F.R. § 1.821 et seq. In addition, the specification has been amended as shown above to incorporate the sequence identifiers where appropriate.

### **35 U.S.C. 112, First Paragraph**

The pending claims were rejected as allegedly containing new matter, namely the recitation "DNA-dependent" to describe the RNA polymerase II. (Office Action, page 3).

Applicants note that satisfying the written description requirement does not require that the precise terms be contained in the specification. Thus, although the term DNA-dependent promoter does not occur *per se* in the application, it was well-known at the time of filing that RNA polymerase II was DNA dependent. Nonetheless, in a sincere effort to advance prosecution, the term has been removed from the claims by amendment herein, thereby obviating this rejection.

### **35 U.S.C. § 103**

All of the pending claims stand rejected as allegedly obvious over U.S. Patent No. 6,015,686 (hereinafter "Dubensky"); Cella et al. (hereinafter "Cella") and U.S. Patent No. 5,736,388 (hereinafter "Chada"). Although it is acknowledged the Dubensky fails to teach a single construct comprising an RNA pol II promoter expressing a heterologous antigen and another promoter encoding a nucleic acid that forms double-stranded RNA, the Office Action

maintains that the claimed subject matter would have been obvious over the combination of Dubensky, Chada and Cella. (Office Action, pages 5-12). In particular, it is maintained that Cella provides the motivation to use a construct encoding both an antigen and double stranded RNA in one construct and that Chada provides the motivation to use multiple promoters. (Office Action, pages 6-9).

Applicants traverse the rejections and supporting remarks.

As a threshold matter, Applicants again note that Dubensky and Chada are both directed to eukaryotic layered vector initiation systems. As acknowledged by the Office, these systems are characterized by the fact that multiple vector constructs are employed, rather than a single one as claimed. For its part, Cella is completely silent as to expression constructs, let alone a construct containing two promoters (one that drives expression of an antigen and the other that drives expression of a non-coding double stranded RNA). Because there is no suggestion in any of the references to combine the individual elements in the claimed arrangement, a *prima facie* case of obviousness cannot be established.

Not only do the references fail to suggest a single vector with the claimed components, they also fail to teach or suggest an expression construct having the claimed components, namely a sequence that, when transcribed, forms double stranded RNA. As repeatedly admitted by the Office, Dubensky and Chada suggest only that multiple heterologous genes can be expressed from the same construct. In contrast, the claimed constructs express at least one non-gene, *i.e.*, a non-coding double stranded RNA. As noted above, Cella does not disclose expression constructs and this reference's showing that dsRNA activates human DCs and influenza infection is a far cry from providing the motivation to arrive the claimed constructs. The Office has not pointed to (and indeed cannot point to) anything in Cella that would lead one of skill in the art to make a single construct encoding both double stranded RNA and an antigen. Simply put, there is no motivation in any of the references to make a single construct encoding both double-stranded RNA and an antigen and, moreover, no reasonable combination of these references that would lead the skilled artisan to the constructs as claimed.

Finally, Applicants address the Examiner's contention that double stranded RNA is equivalent to antisense RNA. In fact, as was known at the time of filing and is made abundantly clear by the specification as filed, double stranded RNA is distinct from antisense RNA. (*See, e.g.*, page 9, lines 8-10 noting that "expression cassettes...can be generated to express double stranded RNA, ribozymes and antisense RNA, as well as antigens..."). Antisense RNA is the term given to a particular sequence of RNA that forms stable duplexes with mRNA or stable triplexes with a portion of a gene (page 7, lines 10-13 of the specification). Unlike antisense RNA, double stranded RNA may be formed by folding of a single molecule of RNA (Figure 1); may be a circularized form a single molecule (Figure 2); or may be "true" double stranded RNA

(Figure 3). Thus, the Examiner's reference to col. 23 of Dubensky, which discloses the inclusion of heterologous antisense-encoding sequences is utterly irrelevant to the claimed constructs, which necessarily include sequences which, when transcribed, form double stranded RNA, not antisense RNA.

Because Dubensky and Chada do not teach or suggest single expression cassettes including sequences that, when transcribed, form double stranded RNA and Cella is completely silent as to expression constructs entirely, there is no motivation in any of the references to arrive at the claimed subject matter. Accordingly, Applicants request that this rejection be withdrawn.

**CONCLUSION**

In view of the foregoing amendments, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

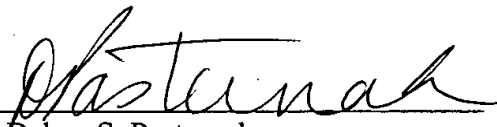
The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §1.16, §1.17, and §1.21, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648, referencing Atty. Docket No. 2302-1631.

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